

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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| Applicant's or agent's file reference VJRB45211 | FOR FURTHER ACTION | See Notification of Transmittal Preliminary Examination Report (Form PCT/PEA/16) | WIBO International PCT |
| International application No. PCTEP 03/06096 | International filing date (day/month/year) 06.06.2003 | Priority date (day/month/year) 11.06.2002 | |
| International Patent Classification (IPC) or both national classification and IPC C07K14/315 | | | |
| Applicant GLAXOSMITHKLINE BIOLOGICALS S.A. | | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.



- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

EPO - DG 1

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

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| Date of submission of the demand 09.12.2003 | Date of completion of this report 04.03.2004 |
| Name and mailing address of the international preliminary examining authority:  European Patent Office D-83591 Munich Tel: +49 89 2369 - 0 Tlx: 523655 opmu d Fax: +49 89 2399 - 4465 | Authorized Officer Mossier, B Telephone No. +49 89 2399-9706  |

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03.06096**

1. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*)

Description, Pages

1-68 as originally filed

Claims, Numbers

1-27 as originally filed

Drawings, Sheets

1-45 as originally filed

Sequence listing part of the description, pages:

1-40, as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 46.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
☒ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).
- (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 26 and 27

because:

☒ the said international application, or the said claims Nos. 26 and 27 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (indicate particular elements below) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer-readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

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|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-27 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-27 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-25 |
| | No: Claims | |

2. Citations and explanations

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International application No. PCT/EP 0306096

see separate sheet

Present application relates to fusion partners which act as immunological fusion partners and as expression enhancers. In particular, the fusion partners contain a choline binding domain (for example, the choline binding of the *Streptococcus pneumoniae* LytA amidase or of the pneumococcal CPL1 lysozyme). Said choline binding domain is modified to include a heterologous T-helper epitope and is fused to antigens which are poorly immunogenic. Fusion proteins as well as the use of said fusion proteins in immunogenic compositions and vaccines and their use in medicine are claimed.

Re item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 26 and 27 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

For the assessment of the present claims 26 and 27 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.1 The following documents were taken into account:

- D1: SANCHEZ-PUELLES J M ET AL: 'IMMOBILIZATION AND SINGLE-STEP PURIFICATION OF FUSION PROTEINS USING DEAE-CELLULOSE' EUROPEAN JOURNAL OF BIOCHEMISTRY, vol. 203, no. 1-2, 1992, pages 153-160, XP001155694 ISSN: 0014-2956

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- D2: CAUBIN J ET AL: 'Choline-binding domain as a novel affinity tag for purification of fusion proteins produced in *Pichia pastoris*' BIOTECHNOLOGY AND BIOENGINEERING, vol. 74, no. 2, 20 July 2001 (2001-07-20), pages 164-171, XP001155696 ISSN: 0006-3592
- D3: KJERRULF M ET AL: 'TANDEM REPEATS OF T HELPER EPITOPES ENHANCE IMMUNOGENICITY OF FUSION PROTEINS BY PROMOTING PROCESSING AND PRESENTATION' MOLECULAR IMMUNOLOGY, ELMSFORD, NY, US, vol. 34, no. 8/9, June 1997 (1997-06), pages 599-608, XP000857056 ISSN: 0161-5890
- D4: ASTORI M ET AL: 'RECOMBINATION FUSION PEPTIDES CONTAINING SINGLE OR MULTIPLE REPEATS OF A UBIQUITOUS T-HELPER EPITOPE ARE HIGHLY IMMUNOGENIC' MOLECULAR IMMUNOLOGY, ELMSFORD, NY, US, vol. 33, no. 13, 1996, pages 1017-1024, XP001028964 ISSN: 0161-5890

- V.2 D1 as well as D2 relate to the single step purification of fusion proteins comprising a choline binding domain as tag. The tagged proteins are then purified on DEAE-matrices.

The subject matter disclosed in D3 refers to the incorporation of T helper epitopes as tandem repeats in chimeric proteins in order to render said proteins more immunogenic and D4 discloses MMTV subunit vaccines that comprise the gp52 glycoprotein or the superantigen fused to single or multiple repeats of an universal T-cell epitope (P30) from tetanus toxin. Histidine tags of glutathione-S-transferase (GST) sequences are further included to facilitate the purification of said recombinant proteins by affinity chromatography.

None of the available prior art documents discloses a fusion protein comprising a choline binding domain and a heterologous promiscuous T helper epitope. Hence, subject matter of claims 1 - 27 is considered as novel and it complies with the requirements of Article 33(1) and (2) PCT.

- V.3 The subject matter referred to in claims 1 - 27 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

The problem to be solved by the present application can be regarded as the provision of a fusion protein that, fused to a heterologous protein acts as an expression enhancer and that is further capable of enhancing the immunogenicity

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of the heterologous protein attached thereto.

The available prior art neither teaches nor suggests the fusion of a choline binding domain and a promiscuous T helper epitope to a heterologous protein in order to solve the above mentioned problem. Hence, the subject matter referred to in claims 1 - 27 appears to be inventive under Article 33(3) PCT.

V.4 The subject matter of claims 1 - 25 is considered industrially applicable. Hence, it meets requirements of Article 33(1) and (4) PCT.

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